Childhood Asthma and Exposure to Traffic and Nitrogen Dioxide

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Background: Evidence for a causal relationship between traffic-related air pollution and asthma has not been consistent across studies, and comparisons among studies have been difficult because of the use of different indicators of exposure.

Methods: We examined the association between traffic-related pollution and childhood asthma in 208 children from 10 southern California communities using multiple indicators of exposure. Study subjects were randomly selected from participants in the Children's Health Study. Outdoor nitrogen dioxide (NO_2) was measured in summer and winter outside the home of each child. We also determined residential distance to the nearest freeway, traffic volumes on roadways within 150 meters, and model-based estimates of pollution from nearby roadways.

Results: Lifetime history of doctor-diagnosed asthma was associated with outdoor NO_2; the odds ratio (OR) was 1.83 (95% confidence interval = 1.04–3.22) per increase of 1 interquartile range (IQR = 5.7 ppb) in exposure. We also observed increased asthma associated with closer residential distance to a freeway (2.22 per IQR; 1.36–3.63) and with model-based estimates of outdoor pollution from a freeway (1.89 per IQR; 1.19–3.02). These 2 indicators of freeway exposure and measured NO_2 concentrations were also associated with wheezing and use of asthma medication. Asthma was not associated with traffic volumes on roadways within 150 meters of homes or with model-based estimates of pollution from nonfreeway roads.

Conclusions: These results indicate that respiratory health in children is adversely affected by local exposures to outdoor NO_2 or other freeway-related pollutants.

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Previous studies have demonstrated a link between outdoor air pollution and the occurrence of symptoms in children already diagnosed with asthma.[1] However, results are not consistent with respect to whether air pollution causes asthma. Most studies have found little evidence to support an association between community-average exposures to air pollution and community asthma prevalence.[2] These study designs failed to account for the variability in exposure resulting from vehicular traffic in urban areas. Asthma has been associated with local variation in traffic patterns within communities in many,[3–7] but not all,[8–11] studies that have examined the impact of local traffic. One possible reason for the inconsistency in these recent studies is the use of different indicators of traffic-related pollution. Some have measured pollutant exposure at home, some have estimated traffic volume near the home, and some have estimated exposure to traffic-related pollutants at home based on dispersion models. Little work has been done to validate estimates of traffic exposure against measured pollution concentrations. Most studies have been conducted in European cities, which differ from U.S. cities in the layout of streets and homes, and also in the relative proportion of diesel- to gasoline-powered vehicles.

We evaluated several commonly available indicators of traffic exposure and compared them with nitrogen dioxide (NO_2) levels measured at the homes of subjects participating in the Children's Health Study. The Children's Health Study was initiated in 1993 with a cohort of school-aged children from 12 southern California communities representing a wide range in air quality. To date, this study has reported associations between air pollution and several outcomes, including lung function,[12–15] respiratory symptoms in asthmatics,[16,17] and asthma incidence.[18] These analyses have relied on com-

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parisons of average health across communities in relation to the pollution levels measured at a central site monitor in each community. In 2000, we conducted a study to measure NO_2 levels at a random sample of children's homes within each of the study communities. We examine how local variation in NO_2 and indicators of exposure to traffic-related pollutants are related to each other, and whether they are associated with lifetime prevalence of asthma and asthma-related outcomes.

METHODS

Study Subjects

In calendar year 2000, we measured outdoor NO_2 levels at the homes of randomly selected participants in the Children's Health Study. Eligible children included those who were originally enrolled as fourth graders (average age = 10 years) in 1993 (cohort 1) or 1996 (cohort 2), with the additional criteria that in 2000, they were still actively participating in the study and had lived in the same home since study enrollment. We excluded 2 of the 12 study communities (Lompoc and Lake Arrowhead) from this study, because neither has any major sources of traffic. From the pool of 890 eligible subjects, we randomly sampled 229 children for NO_2 monitoring. Samplers were deployed outside each home for 2-week periods in the summer and fall of 2000. Valid measurements in both seasons were obtained at 208 (91%) of the homes. Reasons for invalid measurements included lost samplers, subjects who moved, and difficulties with field access or deployment. The study protocol was approved by the Institutional Review Board for Human Studies at the University of Southern California, and informed consent was provided by a parent or legal guardian for all study subjects.

Nitrogen Dioxide Sampling

Ambient NO_2 was sampled with Palmes tubes.[19] These diffusion-based samplers have been widely used in several microenvironmental and personal air quality studies.[20–22] We deployed samplers outside the homes of study subjects, thus avoiding previously identified confounders such as indoor nitrous acid formation, gas stoves, or wall heaters. Samplers were attached at the roofline eaves, signposts, or rain gutters at an approximate height of 2 meters above the ground, oriented in a downward position and protected by an oversized paper cup. Duplicate samplers and field travel blanks were randomly assigned to approximately 10% of the subjects' homes. Samplers were deployed for 2-week periods in both summer (mid-August) and fall (mid-November) in all communities. Deployment across communities was accomplished over a 4-day period at the start of the summer and fall field sampling periods. Within any 1 community, samplers at all locations were deployed within a 4-hour period, and 2 weeks later the samplers were retrieved within a 4-hour period. Samplers were transported to and from the field in cooled portable ice chests. The samplers were prepared for field use and analyzed at the Harvard School of Public Health.

Traffic Exposures

We characterized exposure of each study participant to traffic-related pollutants by 3 metrics: (1) proximity of the residence to the nearest freeway; (2) average number of vehicles traveling within 150 meters of the residence each day, including vehicles on freeways, arterials, major collector roads, and (where available) on minor collector roads; and (3) model-based estimates of traffic-related air pollution at the residence, derived from dispersion models that incorporate distance to roadways, vehicle counts, vehicle emission rates, and meteorologic conditions. Methods used to estimate each of these exposure factors are described subsequently.

Residence addresses were standardized and their locations geocoded using the TeleAtlas database and software (Tele Atlas Inc., Menlo Park, CA, www.na.teleatlas.com). We used the TeleAtlas MultiNet USA database, a comprehensive geo-positioning-satellite-accurate database of roadways, for all analyses because it is more accurate than the standard files available from the U.S. Census. To estimate distance to the nearest freeway, we used ERSI ArcGIS Version 8.3 (ESRI, Redland, CA, www.esri.com) software tools to calculate the distance from each residence to the nearest interstate freeway, U.S. highway, or limited access highway. In these calculations, each direction of travel was represented as a separate roadway, and the "distance to nearest freeway" was the shortest distance from the residence to the middle of the nearest set of lanes of the freeway.

To estimate vehicle counts near homes, annual average daily traffic volumes were obtained from the California Department of Transportation (CALTRANS) Highway Performance Monitoring System for the year 2000. The traffic volumes were transferred from the CALTRANS roadway network to the TeleAtlas networks using previously described methods.[23] The hourly traffic volumes on weekdays and weekend days were estimated from the annual average daily traffic volumes and the average diurnal and day-of-week freeway and nonfreeway traffic variations observed in Southern California. These data were used to calculate the daily average number of vehicles traveling within 150 meters of each residence, weighted by inverse distance from the home to each road. This local traffic density was expressed as traffic volume per square meter.

To obtain model-based estimates of traffic-related pollution exposure, we used the CALINE4 line-source air-quality dispersion model.[24] Principal model inputs included roadway link geometry, link traffic volumes, meteorologic conditions (wind speed and direction, atmospheric stability, and mixing heights), and vehicle emission rates. The 5-year

average joint distributions of wind speeds and directions were obtained from 1 surface-monitoring station in or near each study community. The dispersion model was applied to simulate the transport and dispersion of NO_x as a chemically inert pollutant. Although NO, NO_2, and ozone undergo rapid atmospheric chemical reactions immediately downwind of sources, NO_x can be treated as a chemically inert pollutant for the first hour of transport from sources because the time-scale for NO_x oxidation is 10 to 20 hours in urban atmospheres.[25] Vehicle NO_x emission rates were obtained from the California Air Resources Board's EMFAC2002 vehicle emissions model. Concentrations of NO_2 were estimated by applying the annual average ratio of observed NO_2 to NO_x for each hour of the day (from the community central site monitor) to the CALINE4 model's estimated NO_x concentrations. We estimated the contribution to residential exposure separately for freeway and for nonfreeway traffic.

Ambient NO_2 concentrations in the community are a result of meteorologic transport of pollutants into the community, local point and area source emissions, and local mobile source emissions. The CALINE4 model was used to model NO_2 from local traffic in each community and, therefore, always predicts concentrations lower than the total NO_2 from all sources. Separate regional modeling analysis has indicated that local mobile source emissions contribute 12% to 68% of the average NO_2 in the study communities.[23] For comparison purposes, we also generated exposure assignments based on fine particulate matter (PM) and carbon monoxide (CO) emission factors. Model-based estimates of NO_2, PM, and CO were very highly correlated with one another ($R > 0.90$), indicating that the NO_2-based estimates we use in this article should be considered an estimate of traffic-related pollution in general rather than simply exposure to this specific pollutant.

Questionnaire Data

When we originally enrolled subjects as fourth graders, each subject's parent or legal guardian completed a baseline medical history questionnaire. Asthma was defined as a "yes" response to the question "Has a doctor ever diagnosed your child as having asthma?" This questionnaire was also used to determine whether the child had recently (within the last 12 months) wheezed, recently wheezed during exercise, or was currently using any type of medication to control asthma. Questions about potential risk factors for asthma included parental income or education, environmental tobacco smoke exposure, in utero exposure to maternal tobacco smoking, and presence in the home of mildew, water damage, gas stove, pests, and pets.

Statistical Analysis

We used logistic regression to model the relationship of each traffic measure, including measured NO_2 at the home and the traffic indicators described previously, with baseline asthma prevalence in the 208 study participants. A natural-log transformation of each traffic indicator was used in these analyses, because the distribution of each variable was positively skewed. All models included adjustments for sex, race, Hispanic ethnicity, cohort (whether the subject was enrolled in 1993 or 1996), and indicator variables for study community. We considered separate models for 2-week average NO_2 concentrations measured in summer and in winter and for the 4-week average across seasons. Odds ratios (ORs) for asthma in analyses of measured NO_2 concentrations were scaled to an increase of 5.7 ppb, the average interquartile range (IQR) in 4-week average NO_2 within the 10 communities. ORs for the traffic indicators were also scaled to 1 IQR in exposure (specifically 1.2 km for distance to the nearest freeway; 2720 vehicles per m^2 per day for traffic volumes within 150 meters; and 0.64, 0.49, and 1.27 ppb for model-based estimates of NO_2 from freeways, nonfreeways, and all roads, respectively).

RESULTS

Doctor-diagnosed asthma was reported by 31 (15%) of the 208 children, with variability in prevalence across communities (Table 1). Overall community-average NO_2 levels measured at homes ranged from 12.9 ppb in Atascadero to 51.5 ppb in San Dimas, with similar patterns across communities in summer and winter. The NO_2 levels (average of summer and winter) measured at homes are shown in Figure 1. Within each community, there was substantial variation in NO_2 levels from home to home. Although the amount of variation in NO_2 was generally larger in more polluted communities, there were some exceptions. For example, there was little variation in the relatively high NO_2 community of Mira Loma, whereas there was considerable variation in the lower NO_2 community of Alpine.

The average NO_2 concentration measured at homes was associated with asthma prevalence (Table 2). For each increase of 5.7 ppb in average NO_2, the OR for asthma increased by 1.83 (95% CI = 1.04–3.21). Odds ratios were similar whether based on summer-only (1.55) or winter-only (1.50) measurements. The effect of average NO_2 was of similar magnitude after adjustment for several potential confounders, including socioeconomic status of participants and housing characteristics (Table 2).

Measured NO_2 concentrations at homes were correlated with residential distance from the nearest freeway and with model-based estimates of traffic-related pollution from roadways (Appendix Table, available with the online version of this article). In each community, we observed negative correlations between NO_2 concentration and distance of the home to the freeway. The overall correlation between NO_2 and freeway distance, adjusted for community, was $R = -0.54$. The corresponding correlations of measured NO_2

TABLE 1. Distribution of Lifetime History of Asthma and Measured NO_2 by Community (n = 208)

Community	No.	Asthma (%)	NO_2 (ppb)		
			Summer	Winter	Average†
Alpine (AL)	24	21	20.1	19.0	19.6
Atascadero (AT)	13	23	12.3	13.6	12.9
Lake Elsinore (LE)	22	5	17.6	27.4	22.5
Lancaster (LN)	16	19	16.9	22.0	19.5
Long Beach (LB)	20	10	34.6	50.5	42.5
Mira Loma (ML)	17	12	37.2	48.4	42.8
Riverside (RV)	30	20	37.9	42.8	40.3
San Dimas (SD)	34	15	52.0	51.0	51.5
Santa Maria (SM)	19	16	12.7	17.9	15.3
Upland (UP)	13	8	46.3	36.0	41.2

*Parent report of doctor-diagnosed asthma in the child.
†Mean in each community of NO_2 concentrations measured at homes for 2 weeks each in summer and winter. Average is the 4-week arithmetic average of summer and winter measurements.

with model-based estimates were 0.56 for pollution from freeways and 0.34 for pollution from nonfreeways. In each community, measured NO_2 was more strongly correlated with estimates of freeway-related pollution than with nonfreeway pollution. Measured NO_2 was less correlated with traffic counts within 150 meters of homes (R = 0.24), with inconsistent patterns of correlations from community to community.

Both distance to the freeway and the model-based estimate of freeway-related pollutants were associated with asthma history (Table 3). Asthma prevalence was higher with decreasing distance from the freeway; specifically when comparing the 25th to 75th percentile of freeway distance, the OR was 1.89 (95% CI = 1.19–3.02). For the comparison of 75th to 25th percentile of model-based pollutant exposure from freeways, the OR was 2.22 (1.36–3.63). Asthma was not associated with traffic volumes or with model-based exposure to nonfreeway roads. The associations observed with freeway distance and model-based pollution from freeways were robust to adjustment for all of the potential confounders shown in Table 2 (data not shown).

Measured NO_2 and the 2 freeway-related traffic indicators were also associated with recent wheeze, recent wheeze with exercise, and current use of asthma medication

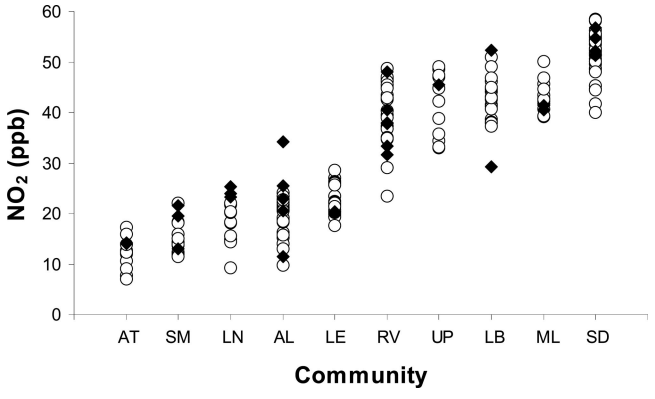

FIGURE 1. Four-week average of nitrogen dioxide measured at homes of asthmatic (solid black diamond) and nonasthmatic (open circle) children in 10 communities. See Table 1 for community abbreviations.

TABLE 2. Association Between 4-Week Average NO_2 at Homes and Asthma History, Adjusted for Several Potential Confounders

Description	OR* (95% CI)
Base model†	1.83 (1.04–3.21)
Base model, with additional adjustment for:	
Environmental tobacco smoke	1.93 (1.09–3.43)
In utero exposure to maternal smoking	1.85 (1.05–3.28)
Parental income	1.99 (1.11–3.57)
Parental education	1.90 (1.07–3.37)
Gas stove	1.87 (1.06–3.30)
Mildew	1.81 (1.01–3.23)
Water damage	1.82 (1.03–3.21)
Cockroaches	1.83 (1.04–3.21)
Pets	1.88 (1.06–3.33)

*Odds ratio per increase of 1 interquartile range (5.7 ppb) in NO_2.
†Base model includes adjustments for sex, race, Hispanic ethnicity, cohort, and community.

TABLE 3. Associations Between Exposure to Traffic at Home and Asthma History

Exposure Metric	Odds Ratio per IQR OR* (95% CI)
Distance to freeway	1.89 (1.19–3.02)
Traffic volume within 150 meters	1.45 (0.73–2.91)
Model-based pollution from:	
Freeways	2.22 (1.36–3.63)
Other roads	1.00 (0.75–1.33)
Freeways and other roads	1.40 (0.86–2.27)

*Odds ratio per change of 1 IQR. For distance to freeway, OR for the 25th percentile compared with the 75th percentile (ie, living closer compared with farther from the freeway). For remaining traffic variables, OR for the 75th percentile compared with the 25th percentile. All models were adjusted for sex, race, Hispanic ethnicity, cohort, and community.

(Table 4). For example, the OR per increase of 5.7 ppb in measured NO_2 was 1.72 (1.07–2.77) for recent wheeze and was 2.19 (1.20–4.01) for current use of asthma medication.

DISCUSSION

We found robust associations of several indicators of exposure to traffic-related air pollution at homes in southern California with lifetime history of asthma, current asthma medication use, recent wheeze, and recent exercise-induced wheeze. Residential distance to a freeway and model-based estimates of freeway traffic-emission exposure at homes were each associated with the prevalence of asthma. Each of these traffic metrics was also correlated with measured concentrations of NO_2, and measured NO_2 was associated with asthma. Taken as a whole, these results indicate that exposure to outdoor levels of NO_2 or other freeway-related pollutants was a significant risk factor for asthma.

A strength of this asthma study is that it used both measured pollution and multiple indicators of exposure to traffic at the same homes in a large number of communities. The results suggest that measuring NO_2 or another pollutant is important for validation of the use of traffic measures and for selection of the most appropriate indicator of traffic exposure for the population under study. Those few studies that have measured residential exposure or that have validated models of exposure using measurements of pollutants have generally shown associations with asthma,[6,7,26] whereas the failure to validate traffic indicators may explain inconsistent results from several other studies.[8–11] In our study, simple distance to a freeway was as strongly and precisely associated with asthma and wheeze as was NO_2. It remains to be seen whether the association with this simple and widely available indicator is replicable in other studies or could be used for estimating risk in communities without having to make additional measurements of traffic-related pollutants.

We did not find associations between respiratory health and other indicators of traffic near homes, including modeled pollution from nonfreeway roads and traffic volumes within 150 meters of homes. One possible explanation for this lack of association is that the contribution to pollution levels from these smaller roads (where tens or hundreds of vehicles travel each day) is trivial compared with freeways that dominate the transportation grid in southern California with daily average counts in our communities between 50,000 to 270,000 vehicles. In addition, vehicle counts are accurately measured on freeways but are only estimated on smaller roads where participants lived. Our results are in contrast to several recent (mostly European) studies that have reported associations of asthma with traffic counts in close proximity to the home.[6,7,27,28] These differences in results may be partly the result of differences in urban geography and closer proximity of homes in Europe to heavily traveled roadways.

There have been a few other studies of traffic and childhood asthma in the United States. One large study in southern California found no association of asthma prevalence with traffic counts within 550 feet of the home,[9] similar to our finding of no association with traffic volumes within 150 meters of the home. Consistent with our findings related to measured NO_2, a recent study in northern California[29] found an association between measured traffic-related pollutants at schools and childhood asthma.

TABLE 4. Associations Between Measured NO_2 and Asthma-Related Outcomes (n = 208)

Outcome	No.	Measured NO_2 OR* (95% CI)	Distance to Freeway OR* (95% CI)	Model-based Pollution From Freeways OR* (95% CI)
Lifetime history of asthma	31	1.83 (1.04–3.22)	1.89 (1.19–3.02)	2.22 (1.36–3.63)
Recent wheeze†	43	1.72 (1.07–2.77)	1.59 (1.06–2.36)	1.70 (1.12–2.58)
Recent wheeze with exercise†	25	2.01 (1.08–3.72)	2.57 (1.50–4.38)	2.56 (1.50–4.38)
Current asthma medication use	26	2.19 (1.20–4.01)	2.04 (1.25–3.31)	1.92 (1.18–3.12)

*Odds ratio per change of 1 IQR in exposure (see footnotes to Tables 2 and 4).
†Within the last 12 months.

The observed associations of traffic with asthma are biologically plausible. Increased oxidative and nitrosative stress associated with NO_2 exposure may impair respiratory responses to infection and thus result in lung injury and asthma exacerbation.[20,30] However, the association of NO_2 with asthma prevalence has been extensively evaluated in epidemiologic studies of exposure to indoor sources, often at levels considerably higher than the modest (5.7 ppb) IQR of exposure in our study, and the observed associations have not been consistent.[30,31] It is possible that outdoor NO_2, which occurs in a complex mixture that includes particulate matter and other pollutants known to affect respiratory health, is a marker of some other traffic-related pollutant(s) responsible for increasing asthma risk. For example, some field studies suggest that the concentration of fine particulate matter, especially black smoke (an indicator of diesel exhaust), varies with nearby high-traffic roads and with NO_2.[32–35] It has been hypothesized that particulate matter, especially diesel exhaust particulate, may contribute to the development of allergies and asthma.[36] Additional research is needed to study the health effects of specific pollutants that occur in complex mixtures of traffic emissions.

A possible limitation of this study is the assessment of asthma by questionnaire, which could be affected by access to care and differences in diagnostic practice among physicians.[37] However, we found associations of traffic indicators with recent wheeze and exercise-induced wheeze, 2 symptoms of asthma that are unlikely to be affected by access to care or diagnostic bias. Another limitation is the possibility of poor or biased reporting of asthma by parents. However, self-report of physician-diagnosed asthma has been found to reflect what physicians actually reported to patients, at least in adults, and validity as assessed by repeatability of response is good.[38] Self-report of physician diagnosis has been the main criterion for identifying asthma in epidemiologic studies of children and has been recommended as the epidemiologic gold standard because a more precise identification tool is not available.[39] Reporting bias is unlikely to have explained the observed associations, because parents were not aware of the specific focus of the study on air pollution at the time the questionnaire was completed. Biased participation with respect to disease status in this substudy is also unlikely, because the prevalence of doctor-diagnosed asthma in the sample of 208 children (15%, Table 1) was not very different from the asthma prevalence in the remaining 668 eligible children (13%, $P = 0.56$).

Another potential study limitation is that measured NO_2 and the traffic metrics were determined after the onset of asthma and extrapolated to earlier in life. However, the systems of freeways and other major roadways in the study communities have been in place and essentially unchanged for many years. We thus expect that the spatial pattern of exposure to traffic emissions from home to home was relatively similar over the lifetimes of these children. Bias could also have occurred if the families of asthmatic children had preferentially moved to a home near a freeway, but this seems unlikely. Additionally, our observed associations were robust to adjustment for factors known to be related to population mobility, housing location, and access to care, including race/ethnicity and indicators of socioeconomic status (as well as household characteristics). This robustness further suggests that our results were not the result of these potential confounders.

These results have both scientific and public health implications. They strengthen an emerging body of evidence that air pollution can cause asthma and that traffic-related pollutants that vary within communities are partly responsible for this association. The current regulatory approach that focuses almost exclusively on regional pollutants merits reevaluation in light of this emerging evidence and in light of the enormous costs associated with childhood asthma.[40] In addition, because NO_2 may be a surrogate for the pollutant or pollutants responsible for the observed effects, further study is indicated to identify the specific pollutant(s). In this regard, improved physical and chemical characterization of ambient ultrafine particles (including particle number concentration distributions, as well as more traditional chemical analyses) are topics of specific ongoing research interest in southern California and elsewhere.

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